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EXAMINER

HUI, SAN MING R

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 10/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/868,063

Applicant(s)

MCKEARN ET AL.

Examiner

San-ming Hui

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,42,43 and 115 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,42,43 and 115 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 1-21-04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Applicant's amendments filed July 1, 2004 have been entered. The restriction requirements are withdrawn in view of the amendments filed July 1, 2004, as the examiner trying to be consistent with the previous office actions.

The cancellation of claims 4-41, 44-114, and 116-158 is acknowledged.

Claims 1-3, 42, 43, and 115 are pending.

The outstanding objection is withdrawn in view of the amendments filed July 1, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, does not reasonably provide enablement for the prevention of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the specification fails to provide sufficient information to enable a person of skilled in the art to practice the instant invention without undue experimentation.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have

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required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApl 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence of absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art
- 7) the predictability of the art, and
- 8) the breadth of the claims.

The claims are very broad.

The term "prevention" can be construed broadly as either preventing the onset of clinically evident neoplasia altogether or preventing the onset of a preclinically evident stage of neoplasia in individuals at risk. In other words, the instant claims are drawn to a method of preventing all preclinical stages of breast cancer, which include any undetectable stages of malignancy. The instant specification also fails to provide any guidance as to selecting the appropriate patient population. It is known in the art that various factors are involved in causing breast cancer in an individual. These factors include genetics, prolonged use of estrogen replacement, age, and environmental factors, such as diet (See Merck Manual, 16th ed., 1992, page 1815-1816). Without sufficient guidance, one of skilled in the art would be required to perform undue experimentation in order to practice the instant invention. Furthermore, the instant

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specification provides no working example of employing integrin antagonist to prevent the development of breast cancer. The nature of the invention is to prevent breast cancer by employing the herein claimed integrin antagonist and tamoxifen together or optionally, further combine with radiation therapy. However, radiation exposure would actually increase risk of developing breast cancer (See Merck Manual, page 1816, last paragraph). It is not clear how or why one of skilled in the art would use radiation therapy on individual who is only at risk for having breast cancer and is otherwise healthy. Moreover, the current known treatment of breast cancer is limited to hormonal, surgical, radiation, and chemotherapy (See Merck Manual, particularly, page 1818 to 1821). There is no preventive treatment so far. It is clear from the evidence of Merck Manual that the ability to prevent breast cancer is highly unpredictable and has met with very little success. Applicants have not provided any convincing evidence that their claimed invention is indeed useful as preventive for breast cancer and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 43 recites the broad recitation "carcinoma", and the claim also recites "clear cell carcinoma", "large cell carcinoma", "metastatic carcinoma", "small cell carcinoma", "soft tissue carcinomas", "squamous carcinoma", "squamous cell carcinoma", "undifferentiated carcinoma", and "well differentiated carcinoma" which are the narrower statement of the range/limitation, the claim also recite "adenoid cystic carcinoma", "adenosquamous carcinoma", "bartholin gland carcinoma", "basal cell carcinoma", "bronchial gland carcinoma", "choroid plexus papilloma/carcinoma", "cholangiocarcinoma", "mucoepidermoid carcinoma", "hepatocellular carcinoma", "oat cell carcinoma", "renal cell carcinoma", "serous carcinoma", "verrucous carcinoma", and "invasive squamous cell carcinoma", which are the narrowest limitations.

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Claim 43 also recites the broad recitation “melanoma”, “malignant melanoma”, and the claim also recites “acral lentiginous melanoma”, “lentigo maligna melanomas”, “superficial spreading melanoma”, and “nueroepithelial adenocarcinoma nodular melanoma”, which are the narrower statement of the limitation.

Claim 43 also recites the broad recitation “sarcoma”, and the claim also recite various sarcoms that are narrower statement of the limitation.

The terms “capillary”, “cavernous”, “ependymal, epitheloid”, pancreatic polypeptide”, “pineal cell”, and “submesothelial” recited in claim 43 are not neoplastic disorders.

The terms “well differentiated carcinoma” and “undifferentiated carcinoma” , “small cell carcinoma”, “metastatic carcinoma”, “large cell carcinoma” recited in claim 43 render the claim indefinite as to what kind of neoplastic disorders encompassed thereby.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 42, 43, and 115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seibert et al. and Santos (Clin. Exp. Metastasis, 1997, 15:499-508).

Seibert teaches celecoxib for treating neoplasia including lung cancer (See claims 1, 5, and 8; also col. 17 and 18) and basal cell carcinoma (See col. 2, lines 47-48). Seibert also teaches COX-2 inhibitors can be administered in conjunction with other antineoplastic agents including paclitaxel (See col. 12, lines 46-47 and 62). Seibert also teaches the administration of the antineoplastic agents can be “in a sequential manner” and “in a substantially simultaneous manner” (See col. 15, lines 19-20, also col. 15, lines 22 and 23).

Santos teaches AG3340 as the most efficacious compounds among the compounds tested in battling Lewis lung carcinoma cell line and murine melanoma cell line, resulting in the complete against primary tumor growth throughout the experiment (See the abstract, and for example page 503, coil. 2 bridging page 504col. 1).

The references do not expressly teach the compounds of Seibert and Santos being used together for treating lung cancer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ all the compounds of Seibert and Santos together for treating lung cancer.

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One of ordinary skill in the art would have been motivated to employ all the compounds of Seibert and Santos together for treating lung cancer. It is generally considered prima facie obvious to combine two compounds each of which is taught by the prior art to be useful for the same purpose, in order to form a composition which is to be used for the very same purpose. The idea for combining them flows logically from their having been used individually in the prior art. As shown by the recited teachings, the instant claims define nothing more than the concomitant use of two conventional medicaments employed to treat lung cancer. Those compounds herein claimed, and taught by the Examiner cited prior art are old and well known for treating lung cancer. It would follow that the recited claims define prima facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980). Furthermore, following the same logic, employing the herein claimed compounds (i.e., Seibert's and Santos') concomitantly, when they are known as effective to treat lung cancer individually, together for treating the very same disorder would also be considered obvious, absent evidence to the contrary (See *In re Kerkhoven* 205 USPQ 1069).

Response to Arguments

Applicant's arguments filed July 1, 2004 averring the cited prior art's teaching away have been considered, but are not found persuasive. Seibert does not exclude the employment of using two more anti-neoplastic agents. In fact, it is well-known in the art that sometimes multiple agents regimens could be used depending on which type of cancers are being treated. Teaching away has to be a positive statement that

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discourage the skilled artisan to arrive at the instant invention. In the instant case, no teaching away is seen because Seibert does not specifically exclude the use of more than two agents together for treating neoplastic disorders.

Applicant's arguments filed July 1, 2004 averring the cited prior art's failure to provide motivation to combine the specific herein claimed combination have been considered, but are not found persuasive. Firstly, examiner notes that the broadest claim does not recite any three specific agents. Secondly, the motivation to combine is based on the fact that the specific agents herein are known to be useful for treating lung cancer, therefore, combining them into a single composition and method useful for treating the very same disorder is considered obvious, absent evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



San-ming Hui
Patent Examiner
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